



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/062,131	02/01/2002	John C. Russell	6885USO1	2508
23492	7590	06/27/2008		
PAUL D. YASGER ABBOTT LABORATORIES 100 ABBOTT PARK ROAD DEPT. 377/AP6A ABBOTT PARK, IL 60064-6008			EXAMINER HAQ, SHAFIQUL	
			ART UNIT 1641	PAPER NUMBER
			NOTIFICATION DATE 06/27/2008	DELIVERY MODE ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Patents_Abbott_Park@abbott.com
Legal_Patents@abbott.com

Office Action Summary	Application No. 10/062,131	Applicant(s) RUSSELL, JOHN C.	
	Examiner SHAFIQL HAQ	Art Unit 1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/18/08</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1 and 30 are pending in the application.
2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/18/08 has been entered.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1 and 30 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Schwartz {US 2003/0013857}.

Schwartz describes a method of attaching a protein to a functionalized solid surface through a hydrazone linkage to form a solid surface-protein complex as described in steps a) through c) of claims 1 and 30 of this application wherein hydrazide-containing macromolecules (e.g. proteins) are immobilized to a functionalized solid support via hydrazone bond formation. Schwartz discloses solid

support modified with hydrazide linkers (see paragraphs [0018], [0112], 0134-0135], [0146-0147] and [0150]) which, when reacted with molecules (e.g. proteins, peptides, polynucleotides) possessing carbonyl group forms hydrozone linked molecules (see paragraphs [0144], [0147], [0148] and [0175]) that are cleavable (paragraph [0110]) i.e. molecules (i.e. proteins, peptides, polynucleotides) linked to a solid support with a cleavable linkages (e.g. hydrazone) are disclosed by Schwartz. Schwartz further discloses that cleavable linkages have been used to isolate receptors (i.e. second macromolecule) following covalent linking between a ligand (i.e. first macromolecule) and a receptor (paragraphs [0109] and [0110]). Schwartz also discloses binding of antibody (i.e. first macromolecule) to hydrazide modified surface using carbohydrate domain of the antibody (that is not involved in antigen binding) to form a hydrazone or oxyamino bond and thus keeping the antibody active site available for binding with antigen (second macromolecule) (paragraph [0180]).

The Schwartz method does not specifically describe a step corresponding to step d) of claims 1 and 30 of this application wherein the protein ('First Macromolecule') is covalently linked to another protein ('Second Macromolecule") and cleaving the first macromolecules from the surface without cleaving the covalent bond between the first macromolecules and the at least one second macromolecule.

Given the fact the biomolecules (binding partners e.g. antibody, receptors) can be linked to solid support through acid cleavable hydrazone linkages (e.g. hydrazone bond) (Schwartz et al.) and given the generic discussion that other conventional methods are known for covalently linking biomolecules to one another as in the

example of Schwartz wherein biomolecules linked to solid support can be linked to other proteins or analytes (e.g. antigen) by conventional methods (i.e. different covalent bonding), it would be obvious to one of ordinary skill in the art at the time the invention was made to use the hydrazine modified support of Schwartz to immobilize a binding partner (e.g. antibody or ligand i.e. first macromolecule) through a cleavable linkage (e.g. hydrazone) to capture complementary binding partner (e.g. antigen or receptor i.e. second macromolecule) for subsequent cleavage of the binding complex from the solid surface for purification or for further analysis.

The limitation of claim 30 of this application, i.e. the "First Molecule having a molecular weight of at least 2,000 daltons", relates to a molecular weight range conventionally associated with antibodies (a class of proteins).

Response to Argument

5. Applicant's arguments filed August 09, 2007 regarding the Schwartz patent have been fully considered but they are not persuasive to overcome the rejection under 35 USC 103.

Applicant argued that in present application the linker between the first macromolecule and the solid support is cleavable while the linker between the first macromolecule and the at least second macromolecule is not cleavable and argued that if the bond between the First macromolecule and the second macromolecules were cleavable, the conjugate would no longer exist after the complex comprising

the first macromolecules and the second macromolecules is detached from the solid support. Applicants argued that Schwartz does not describe the preparation of conjugates comprising two macromolecules using conventional bifunctional reagents. Applicants further argued that Schwartz teaches away from the method described herein because Schwartz calls for the cleavage of the first macromolecule (protein) from the second macromolecule (protein), which cleavage would destroy the conjugate. Applicants further argued that both a cleavable linker and a non-cleavable linker are required in the method described herein, and Schwartz fails to disclose or suggest the use of a non-cleavable linker.

Applicants' arguments have been fully considered but are not found convincing. In response to Applicants statement that in present application "the linker between the first macromolecules and the solid support is cleavable while the linker between the first macromolecule and the at least second macromolecule is not cleavable", it is noted that the features upon which applicant relies (i.e. the linker between the first macromolecules and the solid support is cleavable while the linker between the first macromolecule and the at least second macromolecule is not cleavable) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The claims recite that a covalent bond exists between the first macromolecule and the second macromolecule but do not recite that the bond is not cleavable. The claims disclose disruption of the bond between the reactive surface and the first macromolecule

without disrupting the covalent bond existing between the first macromolecule and the at least one second macromolecule, but this does not mean that the bond is not cleavable. The bond between the first macromolecule and the second macromolecule is not limited to a particular covalent bond and thus a condition (i.e. reaction condition) at which it disrupts the bond between the first macromolecule may not disrupt the bond between the first macromolecule and the second macromolecule but at other condition it may be disruptable (i.e. cleavable).

With regard to bifunctional reagent, Schwartz teaches aliphatic and aromatic crosslinking compounds comprising various functionalities (see paragraphs 0007, 0008 and 0012) which would encompass different conventional and non-conventional linkers/bonds and the bond between the macromolecules is not limited to a particular type of bond. It is not the bond/linkers itself that determines cleavage, the reaction condition is also important which determines what type of bonds/linker would be cleavable. As for example, if a first biomolecule is linked to a surface through a thiol (e.g. gold-sulfur) bond and the second biomolecule is attached to the first biomolecules through a photocleavable bond or a hydrazino bond, then a reaction condition that breaks the gold-sulfur bond would not cleave the photocleavable bond or the hydrazine bond and similarly, a condition that cleaves the photocleavable bond or hydrazino bond between the may not be suitable to cleave the gold-sulfur bond.

With regard to Schwartz's disclosure of macromolecular complex, Schwartz discloses solid support modified with hydrazide linkers (see paragraphs [0018],

[0112], [0134-0135], [0146-0147] and [0150]) which, when reacted with molecules (e.g. proteins, peptides, polynucleotides) possessing carbonyl group forms hydrozone linked molecules (see paragraphs [0144], [0147], [0148] and [0175]) that are cleavable (paragraph [0110]) i.e. molecules (e.g. proteins, peptides, polynucleotides) linked to a solid support with a cleavable linkage. Schwartz teaches different cleavable linkages such as acid cleavable, photocleavable and disulfide bonds (column 0109) and teaches that the cleavable linkages can be used to isolate receptors following covalent linking between a ligand and a receptor (paragraphs [0109] and [0110]). Schwartz teaches solid support for immobilization of biomolecules and the immobilized biomolecules may be used in diagnostic and therapeutic application (paragraph 0018). Schwartz specifically teaches conjugates comprising protein conjugate with bacterial polysaccharide to be used as vaccine, which does teach macromolecules “conjugated together” and which does not call for the cleavage of the first macromolecule (i.e protein) from the second macromolecule (i.e. bacterial polysaccharide) (paragraph 0017) as Applicants argued and therefore, Schwartz does not teaches away having conjugated macromolecules separated from solid phase.

Therefore, given the fact the biomolecules can be linked to solid support through cleavable linkages (Schwartz et al.) and given the generic discussion that other conventional methods are known for covalently linking biomolecules to one another as in the example of Schwartz wherein biomolecules linked to solid support can be linked to other proteins or analytes (e.g. antigen) by conventional methods, it would

be obvious to one of ordinary skill in the art to immobilize a biomolecule (e.g. antibody, receptor or proteins) through a cleavable linkage to solid phase to capture complementary binding partner (e.g. antigen or ligand) or to bind to carriers (such as in the case of protein polysaccharide conjugate) for subsequent cleavage of the binding complex from the solid surface for further diagnostic and therapeutic applications. From the teaching of cleavable attachment of biomolecules on solid support (Schwartz *et al*), one of ordinary skill in the art can easily envision preparing the conjugate vaccine (i.e. conjugate of a protein with a bacterial polysaccharide) first on a solid support and then cleaving the conjugate from the solid support because this process would require less step to acquire the conjugate vaccine. It is the examiner's position that given the Schwartz discussion of the applicability of the cleavable linkage technology to the conjugation of a wide variety of reactants such as solid surfaces and biomolecules as discussed above, the sequential attachment of a "Second Macromolecule" to a surface-immobilized "First Macromolecule", as claimed, would constitute a routine variation in the sequence of performance of a known set of steps conventionally used to attach biomolecules to each other and/or to solid surfaces via acid cleavable hydrazone bonds as described by Schwartz.

Further, prior art is not limited just to the references being applied, but includes the understanding of one of ordinary skill in the art. The prior art reference (or references when combined) need not teach or suggest all the claim limitations. The "mere existence of differences between the prior art and an invention does not establish the invention's nonobviousness." The gap between the prior art and the

claimed invention may not be “so great as to render the [claim] non-obvious to one reasonably skilled in the art.” In determining obviousness, neither the particular motivation to make the claimed invention nor the problem the inventor is solving controls. The proper analysis is whether the claimed invention would have been obvious to one of ordinary skill in the art after consideration of all the facts. Factors other than the disclosures of the cited prior art may provide a basis for concluding that it would have been obvious to one of ordinary skill in the art to bridge the gap.

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shafiquel Haq whose telephone number is 571-272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Application/Control Number: 10/062,131
Art Unit: 1641

Page 10

/Shafiqul Haq/
Examiner, Art Unit 1641